Use of Oral Glucose Tolerance Test and Glycated Haemoglobin at 20 Weeks of Gestation or Less to Predict or Exclude Subsequent Development of Gestational Diabetes Mellitus in the Current Pregnancy in High-risk Patients

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Objective: To determine cutoff values of oral glucose tolerance test (OGTT) and/or glycated haemoglobin at ≤20 weeks of gestation that could predict or exclude subsequent development of gestational diabetes mellitus (GDM) in the current pregnancy in high-risk patients.
Methods: Retrospective review of all non-diabetic pregnant women who had undertaken 75 g OGTT at ≤20 weeks of gestation in Queen Elizabeth Hospital, Hong Kong, from 1 April 2011 to 30 September 2011, was performed. Gestational diabetes mellitus was diagnosed in accordance with the 1999 World Health Organization criteria. If early OGTT results were normal, second OGTT was performed at 24 to 30 weeks. Sensitivity, specificity, positive predictive value, negative predictive value of the cutoff values, and proportion of OGTTs that could be spared at 24 to 30 weeks of gestation were calculated.
Results: In all, 58 (26%) pregnant women were diagnosed to have GDM by the first OGTT; 45 (30%) women with normal first OGTT had GDM diagnosed by the second OGTT, with higher mean 2-hour plasma glucose level than those in the non-GDM group ($p<0.05$). The best cutoff value that excluded GDM was 2-hour plasma glucose level of <4.4 mmol/L, which spared 5.3% of second OGTTs. The sensitivity, specificity, positive predictive value, and negative predictive value were 100%, 92.8%, 32.3% and 100%, respectively.
Conclusion: Approximately 5.3% of OGTTs at 24 to 30 weeks of gestation among women with multiple risk factors for GDM may be omitted using a 2-hour plasma glucose cutoff value of <4.4 mmol/L in early pregnancy, provided that there is no onset of new risk factor(s) after the first OGTT.
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Introduction

Gestational diabetes mellitus (GDM) is defined as hyperglycaemia with onset of pregnancy or hyperglycaemia if first recognised during pregnancy[1]. It is a common condition with a prevalence of 14.2% in Hong Kong, in contrast to 2% to 7% in the Caucasian population[2,3]. If untreated, it can result in sudden intrauterine fetal death (IUFD), macrosomia and associated birth trauma, preterm delivery, or respiratory distress syndrome. It is also associated with obesity and diabetes mellitus (DM) later in the baby's life[4]. Moreover, pre-GDM or early-onset GDM is associated with an increased risk of development of fetal anomalies and fetal loss[5].

The 1999 World Health Organization (WHO) recommendation of 75 g oral glucose tolerance test (OGTT) is the preferred diagnostic test in Hong Kong. Women are screened for the presence of risk factors at their first visit. If there are two or more risk factors, OGTT is performed shortly after the first visit and then again at 28 to 30 weeks of gestation[5]. Oral glucose tolerance test is inexpensive and has reasonable sensitivity. However, repeated blood taking is inconvenient for patients. Side-effects such as nausea, vomiting, and headache due to administration of glucose solution may also cause discomfort to patients. Some patients may decline a second OGTT because of unpleasant experience during their first OGTT and if that test showed a

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normal result.

Glycated haemoglobin (HbA1c) can be used to reflect glucose control over the previous months because erythrocytes have a constant lifespan and are freely permeable to glucose. The haemoglobin glycation process is non-enzymatic and the rate is directly proportional to the ambient glucose concentration. An expert committee suggested the use of HbA1c value of ≥6.5% to diagnose DM outside pregnancy[6]. Some studies have shown that HbA1c could reduce the need for OGTT in diagnosing GDM[7,8]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) used HbA1c value of ≥6.5% to diagnose overt DM in pregnancy[9], but other authorities do not recommend its application in pregnant women[10,11].

It is postulated that a normal OGTT with glucose level close to the cutoff value for GDM may reflect cases that may convert to GDM in later stages of pregnancy due to increased insulin resistance. If results of OGTT or HbA1c in early pregnancy could predict or exclude the subsequent development of GDM in the current pregnancy, then subsequent OGTTs may be omitted in selected high-risk women. Moreover, early screening for GDM at the time of Down's screening in the first trimester instead of at 24 to 28 weeks of gestation may allow early commencement of lifestyle modification and treatment before development of diabetic complications, and may reduce the need for repeated blood taking. On the other hand, if the first blood taking predicts a high risk of subsequent development of GDM, a repeated OGTT will be required even if the patient is regarded as low risk by the existing criteria. Therefore, this study aimed to determine whether OGTT and/or HbA1c results at ≤20 weeks of gestation in high-risk group of patients could predict or exclude subsequent development of GDM in the current pregnancy, and to determine the cutoff values of the tests.

Methods

This retrospective observational study included all non-diabetic pregnant women who had undertaken 75 g OGTT at ≤20 weeks of gestation in Queen Elizabeth Hospital, Hong Kong, from 1 April 2011 to 30 September 2011.

The protocol of GDM screening in Queen Elizabeth Hospital was as follows. Women with one risk factor (excluding ethnicity) were routinely screened by 75 g OGTT as close to 28 weeks of gestation as possible (24 to 30 weeks). Those with two or more risk factors were screened by 75 g OGTT in early pregnancy after the initial booking visit and then again at 24 to 30 weeks. Those who had developed new risk factors undertook OGTT as soon as feasible. Risk factors in the departmental protocol were as follows: advanced maternal age (AMA; maternal age ≥35 years), a family history of DM, maternal obesity at booking with body weight of ≥80 kg or body mass index (BMI) of ≥28 kg/m^2, known polycystic ovarian syndrome (PCOS), history of GDM or impaired glucose tolerance (IGT) in previous pregnancy, a history of IUFD or stillbirth, a history of macrosomia ≥4 kg, multiple pregnancy, large for gestational age fetus or polyhydramnios on antenatal ultrasound, maternal use of medications (such as corticosteroids), and excessive weight gain during pregnancy (at the discretion of the managing obstetrician).

Gestational diabetes mellitus was diagnosed in accordance with the 1999 WHO criteria, by fasting plasma glucose (FPG) level of ≥7.0 mmol/L and/or 2-hour plasma glucose (PG) level of ≥7.8 mmol/L after a 75 g OGTT. No further OGTTs were performed when a patient was diagnosed to have GDM. The hospital laboratory used high-performance liquid chromatography for HbA1c quantification with the VARIANT II machine (Bio-Rad, California, US). Glycated haemoglobin level was represented in percentage. Glucose measurement was performed by hexokinase and ultraviolet detection of glucose with the Modular D System (Roche, Indianapolis, US). Both tests were performed in a laboratory with accreditation of the National Association of Testing Authorities/Royal College of Pathologists of Australasia.

Women with pre-existing DM, with incomplete results, and at risk but who did not perform OGTT in the day centre were excluded from the study. Women with second OGTT performed before 24 weeks of gestation were excluded because normal glucose tolerance at that stage might not exclude the subsequent development of GDM. Women with change in risk factor(s) for GDM between two tests were also excluded because it is more appropriate to have repeated OGTT if there is onset of new risk factor(s), regardless of the previous OGTT results. In addition, women with uncertain or known variant haemoglobinopathies such as thalassemia trait were excluded during analysis of HbA1c and cutoff values, as variant haemoglobin patterns might affect the result[12].

Statistical analysis was performed by the SPSS Windows version 19.0. Independent sample *t* test and Chi-square test were used to analyse the parametric and non-parametric data, respectively. Logistic regression test and

receiver operating characteristic (ROC) curve were used to assess the performance of the parameters in predicting GDM. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of the cutoff values, and proportion of OGTTs that could be omitted at 24 to 30 weeks of gestation were calculated.

Based on a similar study[13], the mean (± standard deviation) FPG values at ≤16 weeks of gestation were 5.4 ± 0.7 mmol/L, 4.9 ± 0.5 mmol/L, and 4.6 ± 0.4 mmol/L for those with GDM diagnosed at 24 to 28 weeks, GDM diagnosed at 32 to 34 weeks, and without GDM, respectively. To detect the smallest potential difference between GDM and non-GDM groups, mean FPG level of 4.9 mmol/L was used to represent the GDM group in order to calculate the sample size. Assuming 5% significance level and 80% power, the number of cases in each group was 36. The mean 2-hour PG values were 7.1 ± 0.4 mmol/L, 6.2 ± 1.2 mmol/L, and 5.5 ± 1.0 mmol/L for those with GDM diagnosed at 24 to 28 weeks, GDM diagnosed at 32 to 34 weeks, and without GDM, respectively. Based on the same rationale, the number of cases in each group was 40.

The study was performed according to the guidelines set forth in the current version of the Declaration of Helsinki. A review of medical records, which were already existing as part of clinical care, posed no physical risks. Therefore, consent from the patients was not obtained. Data were recorded in a manner that did not allow the participants to be identified; a non-recognisable code was assigned to each participant. The study protocol was approved by the Research Ethics Committee (Kowloon Central/Kowloon East).

Results

A total of 223 pregnant women undertook OGTTs at ≤20 weeks of gestation during the study period, accounting for approximately 6.4% of antenatal new case bookings during the same period. Of these, data of 14 women were excluded because of various reasons (Figure 1). Thus, data

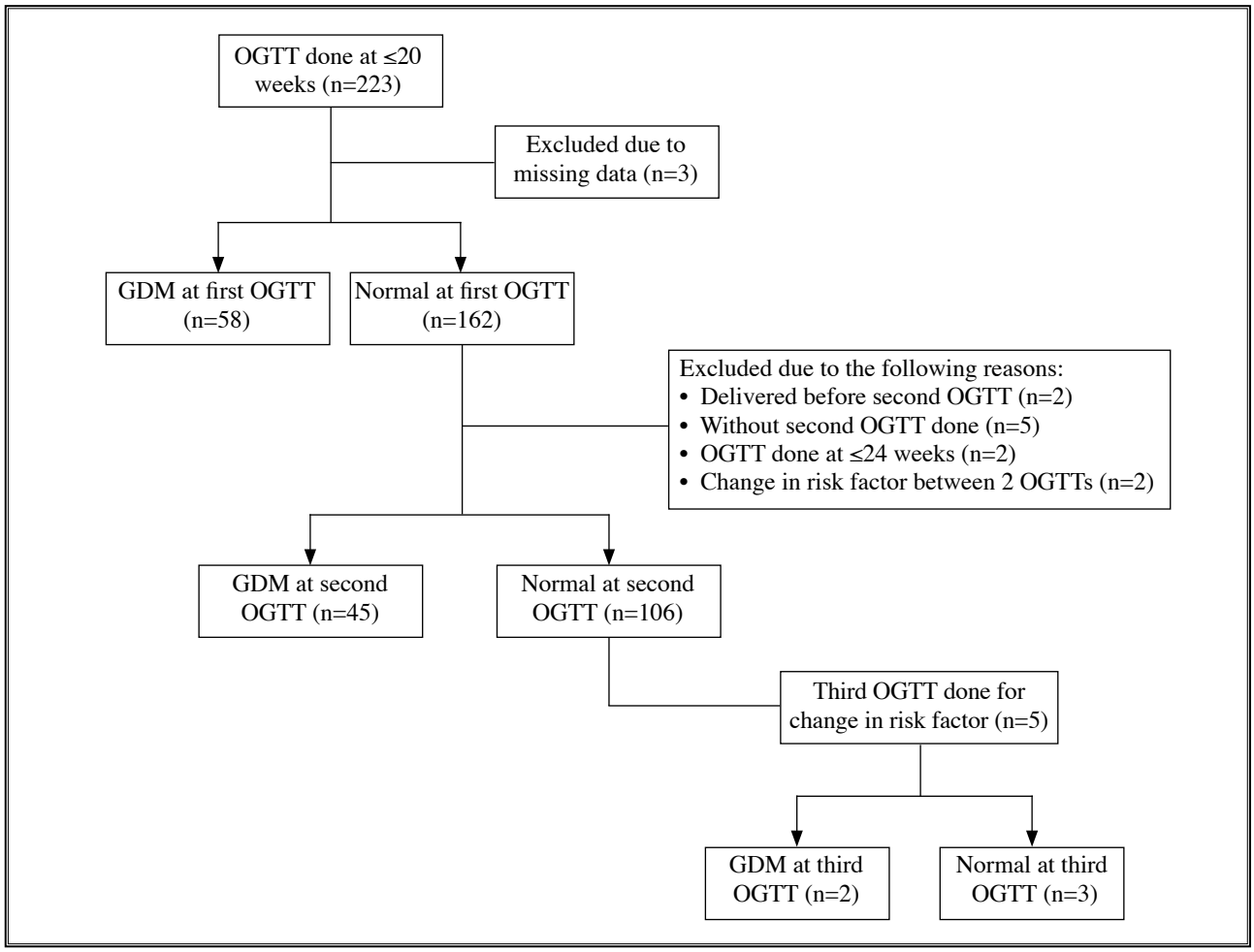

Figure 1. Distribution of study subjects
Abbreviations: GDM = gestational diabetes mellitus; OGTT = oral glucose tolerance test

from the remaining 209 women were analysed. Overall, 105 (50%) women were diagnosed to have GDM at first (n=58), second (n=45), and third (n=2) OGTT. Baseline characteristics of women with and without GDM are compared in Table 1. More women in the GDM group had a history of GDM or IGT in their previous pregnancy, as well as more than two risk factors when compared with those in the non-GDM group. Both the mean FPG and 2-hour PG levels at first OGTT in the GDM group were significantly higher than those in the non-GDM group (4.5 mmol/L vs. 4.4 mmol/L, p=0.01 for FPG; and 7.9 mmol/L vs. 6.0 mmol/L, p<0.001 for 2-hour PG), but not the mean HbA1c level (5.5% vs. 5.4%; p=0.06).

When comparing women with GDM diagnosed by first and second OGTTs (Table 2), no differences in baseline characteristics and risk factors were noted. The mean 2-hour PG at first OGTT was higher in those with GDM diagnosed by first OGTT compared with those diagnosed by second OGTT (9.1 mmol/L vs. 6.4 mmol/L; p<0.001). However, there were no statistically significant differences in the mean FPG and HbA1c values between the two groups (4.6 mmol/L vs. 4.5 mmol/L, p=0.51 for FPG and 5.5% vs. 5.5%, p=0.96 for HbA1c).

Among women with normal first OGTT, the incidence of GDM diagnosed by second OGTT was 30%; more women in this group had more than two risk factors when compared with the non-GDM group. Otherwise, there were no differences in baseline characteristics and timing of performing OGTT between the groups (Table 3). The mean 2-hour PG at first OGTT was higher in the GDM

Table 1. Comparison of demographic data among women with and without GDM

Demographics	With GDM (n = 105)	Without GDM (n = 104)	p Value
Age at delivery (years)	36.3 ± 3.2	36.3 ± 3.0	0.95
Parity			0.28
0	34 (32%)	42 (40%)	
1	62 (59%)	50 (48%)	
≥2	9 (9%)	12 (12%)	
Ethnicity			0.22
Chinese	98 (93%)	92 (89%)	
Asian non-Chinese	7 (7%)	12 (12%)	
Mean (± SD) BMI (kg/m^2)	23.8 ± 4.8	22.9 ± 4.6	0.15
AMA	83 (79%)	92 (89%)	0.07
Obesity	21 (20%)	15 (14%)	0.29
PCOS	2 (2%)	2 (2%)	1.00
Previous GDM / IGT	31 (30%)	17 (16%)	0.02
Family history of DM	80 (76%)	81 (78%)	0.77
Previous big baby	9 (9%)	3 (3%)	0.13
Previous IUFD / SB	2 (2%)	1 (1%)	1.00
Multiple pregnancy	11 (11%)	6 (6%)	0.21
Medication use	1 (1%)	3 (3%)	0.37
Presence of >2 risk factors	30 (29%)	13 (13%)	0.004
Mean (± SD) first OGTT (mmol/L)			
FPG	4.5 ± 0.7	4.4 ± 0.4	0.01
2-Hour PG	7.9 ± 1.9	6.0 ± 1.0	<0.001
Mean (± SD) first HbA1c (%)	5.5 ± 0.4 (n = 94)	5.4 ± 0.3 (n = 97)	0.06

Abbreviations: AMA = advanced maternal age; BMI = body mass index; DM = diabetes mellitus; FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; IGT = impaired glucose tolerance; IUFD = intrauterine fetal death; OGTT = oral glucose tolerance test; PCOS = polycystic ovarian syndrome; PG = post-glucose; SB = stillbirth; SD = standard deviation

Table 2. Comparison of characteristics among women with GDM diagnosed at first and second OGTT

Characteristic	GDM at first OGTT (n = 58)	GDM at second OGTT (n = 45)	p Value
Age at delivery (years)	35.8 ± 3.4	36.9 ± 2.9	0.11
Parity			1.00
0	18 (31%)	15 (33%)	
1	35 (60%)	27 (60%)	
≥2	5 (9%)	3 (7%)	
Ethnicity			0.13
Chinese	52 (90%)	44 (98%)	
Asian non-Chinese	6 (10%)	1 (2%)	
BMI (kg/m^2)	24.3 ± 4.7	23.1 ± 5.0	0.22
AMA	42 (72%)	39 (87%)	0.08
Obesity	15 (26%)	6 (13%)	0.12
PCOS	2 (3%)	0	0.50
Previous GDM / IGT	20 (35%)	11 (24%)	0.27
Family history of DM	44 (76%)	34 (76%)	0.97
Previous big baby	6 (10%)	3 (7%)	0.73
Previous IUFD / SB	2 (3%)	0	0.50
Multiple pregnancy	4 (7%)	7 (16%)	0.20
Medication use	0	1 (2%)	0.44
Presence of >2 risk factors	18 (31%)	12 (27%)	0.63
Gestation at first OGTT (weeks)	15.4 ± 2.3	15.3 ± 2.2	0.89
Mean (± SD) first OGTT (mmol/L)			
FPG	4.6 ± 0.8	4.5 ± 0.5	0.51
2-Hour PG	9.1 ± 1.5	6.4 ± 1.0	<0.001
Mean (± SD) first HbA1c (%)	5.5 ± 0.4 (n = 49)	5.5 ± 0.3 (n = 43)	0.96

Abbreviations: AMA = advanced maternal age; BMI = body mass index; DM = diabetes mellitus; FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; IGT = impaired glucose tolerance; IUFD = intrauterine fetal death; OGTT = oral glucose tolerance test; PCOS = polycystic ovarian syndrome; PG = post-glucose; SB = stillbirth; SD = standard deviation

group compared with the non-GDM group (6.4 mmol/L vs. 6.0 mmol/L; p=0.01) [Table 4]. There were no statistically significant differences in mean FPG (4.5 mmol/L vs. 4.4 mmol/L; p=0.05) and HbA1c (5.5% vs. 5.4%; p=0.12) values at first OGTT between the groups.

The ROC curves of the FPG, 2-hour PG, and HbA1c at first OGTT are shown in Figure 2. The area under the curve (AUC) values for FPG, 2-hour PG, and HbA1c were 0.60, 0.66 and 0.57, respectively. Only AUC of FPG was statistically significant. Logistic regression analysis showed that the strongest predictor of GDM among the blood results was 2-hour PG with odds ratio of 1.83 (95% confidence interval, 1.20-2.79; p=0.01), while the others were not statistically significant (Table 5).

In view of potential consequence of missing a case of GDM, cutoff values with high NPV were chosen to exclude a diagnosis of GDM. The cutoff values alone or in combination are shown in Table 6. Second OGTT could be omitted if the results were below the cutoff values. The best cutoff value to exclude GDM was 2-hour PG of 4.4 mmol/L, which spared 5.3% of OGTTs without missing a case of GDM. The sensitivity, specificity, PPV, and NPV were 100%, 92.8%, 32.3% and 100%, respectively.

High PPV and specificity should be used to determine cutoff values that predict GDM, above which the second OGTT could be omitted. The cutoff values derived are shown in Table 7. Additional cutoff values of 5.1 mmol/L for FPG and 6.5% for HbA1c were also analysed,

Table 3. Baseline characteristics of women with normal first OGTT

Characteristic	GDM at second OGTT (n = 45)	Normal at second OGTT* (n = 104)	p Value
Age at delivery (years)	36.9 ± 2.9	36.3 ± 3.0	0.29
Parity			0.37
0	15 (33%)	42 (40%)	
1	27 (60%)	50 (48%)	
≥2	3 (7%)	12 (12%)	
Ethnicity			0.11
Chinese	44 (98%)	92 (89%)	
Asian non-Chinese	1 (2%)	12 (12%)	
Mean (± SD) BMI (kg/m^2)	23.1 ± 5.0	22.9 ± 4.6	0.75
AMA	39 (87%)	92 (89%)	0.76
Obesity	6 (13%)	15 (14%)	0.86
PCOS	0	2 (2%)	1.00
Previous GDM / IGT	11 (24%)	17 (16%)	0.25
Family history of DM	34 (76%)	81 (78%)	0.76
Previous big baby	3 (7%)	3 (3%)	0.37
Previous IUFD / SB	0	1 (1%)	1.00
Multiple pregnancy	7 (16%)	6 (6%)	0.05
Medication use	1 (2%)	3 (3%)	1.00
Presence of >2 risk factors	12 (27%)	13 (13%)	0.03
Mean (± SD) gestation at first OGTT (weeks)	15.3 ± 2.2	15.4 ± 1.7	0.84
Mean (± SD) gestation at second OGTT (weeks)	28.2 ± 1.0	28.0 ± 0.6	0.07
Mean (± SD) duration between 2 tests (weeks)	12.9 ± 2.4	12.6 ± 1.8	0.44

Abbreviations: AMA = advanced maternal age; BMI = body mass index; DM = diabetes mellitus; GDM = gestational diabetes mellitus; IGT = impaired glucose tolerance; IUFD = intrauterine fetal death; OGTT = oral glucose tolerance test; PCOS = polycystic ovarian syndrome; SB = stillbirth; SD = standard deviation

* Two patients with GDM diagnosed at third OGTT were excluded

Table 4. OGTT and HbA1c values in women with normal first oral glucose tolerance test*

	GDM at second OGTT (n = 45)	Normal at second OGTT (n = 104†)	p Value
First OGTT (mmol/L)			
FPG	4.5 ± 0.5	4.4 ± 0.4	0.05
2-Hour PG	6.4 ± 1.0	6.0 ± 1.0	0.01
First HbA1c (%)	5.5 ± 0.3 (n = 43)	5.4 ± 0.3 (n = 97)	0.12
Second OGTT (mmol/L)			
FPG	4.7 ± 0.4	4.4 ± 0.4	<0.001
2-Hour PG	8.7 ± 0.8	6.2 ± 1.1	<0.001
Second HbA1c (%)	5.5 ± 0.3 (n = 43)	5.3 ± 0.3 (n = 97)	0.01

Abbreviations: FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; OGTT = oral glucose tolerance test; PG = post-glucose

* Data are shown as mean ± standard deviation

† Two patients with GDM diagnosed at third OGTT was excluded

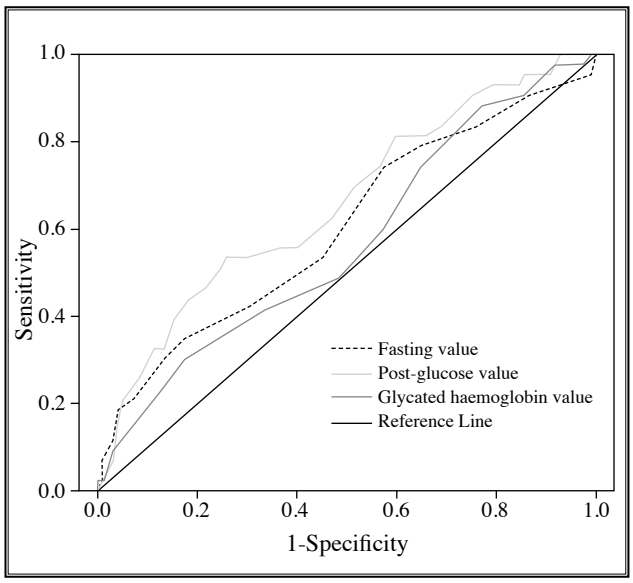

Figure 2. Receiver operating characteristic curves for first fasting plasma glucose, 2-hour post-glucose, and glycated haemoglobin

as these were used to diagnose GDM at the first antenatal visit according to the IADPSG criteria[9]. All the cutoff values were not useful as they spared a limited number of OGTTs while leading to over-treatment of a significant number of women without GDM.

Discussion

This study demonstrated high incidence of GDM in women with two or more risk factors. The mean FPG and 2-hour PG values in early pregnancy were higher in the GDM group compared with the non-GDM group. Among those with normal OGTT in early pregnancy, the mean 2-hour PG values in early pregnancy were higher in the group with GDM diagnosed by second OGTT versus the non-GDM group. However, the 2-hour PG results were of limited use in predicting GDM in the later stage of pregnancy because the AUC value was not high (0.66). We found that 5.3% of second OGTTs could be omitted if

Table 5. Logistic regression analysis of oral glucose tolerance test and glycated haemoglobin values predicting gestational diabetes mellitus

	Coefficient (standard error)	p Value	Odds ratio (95% confidence interval)
FPG	0.80 (0.50)	0.11	2.23 (0.83-5.96)
2-Hour PG	0.60 (0.22)	0.01	1.83 (1.20-2.79)
HbA1c	0.72 (0.62)	0.24	2.06 (0.61-6.93)

Abbreviations: FPG = fasting plasma glucose; HbA1c = glycated haemoglobin; PG = post-glucose

Table 6. Cutoff values at first OGTT that excluded GDM

Cutoff value	Sensitivity	NPV	OGTT spared	GDM missed
FPG (4.2 mmol/L)	79.1%	79.1%	30.7%	20.9%
2-Hour PG (4.4 mmol/L)	100%	100%	5.3%	0%
HbA1c (4.5%)	100%	100%	0.7%	0%
2-Hour PG (6.2 mmol/L) and HbA1c (5.0%)	100%	100%	5.0%	0%

Abbreviations: FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; NPV = negative predicted value; OGTT = oral glucose tolerance test; PG = post-glucose

Table 7. Cutoff values at first OGTT that predicted gestational diabetes mellitus

Cutoff value	Specificity	PPV	OGTT spared	Over-treated
FPG (≥6.0 mmol/L)	100%	100%	0.7%	0%
2-Hour PG (≥7.5 mmol/L)	95.8%	64.3%	10.0%	5.2%
HbA1c (≥5.9%)	96.9%	57.1%	5.0%	3.1%
FPG (≥5.1 mmol/L)	96.9%	75%	2.9%	1.0%
HbA1c (≥6.5%)	100%	100%	0.7%	0%

Abbreviations: FPG = fasting plasma glucose; HbA1c = glycated haemoglobin; OGTT = oral glucose tolerance test; PG = post-glucose; PPV = positive predicted value

2-hour PG value was <4.4 mmol/L at first OGTT. There was no useful cutoff value to predict development of subsequent GDM in the current pregnancy without over-treating women without GDM.

The prevalence of GDM diagnosed by the WHO criteria was 14.2% according to a local study in 2002[2]. The incidence of GDM in this study was 50%. The high incidence in this study was due to inclusion of women with multiple risk factors for GDM. All the patients were Asians and the majority of patients (93%) were of Chinese ethnicity, which itself was a risk factor for GDM. A study in Hungary also showed incidence of 54% in high-risk women[13].

Among women who had GDM or IGT in their previous pregnancy, the possibility of unrecognised glucose intolerance antedating the current pregnancy could not be excluded, as they might not have undergone postpartum glucose tolerance test in the previous pregnancy. This may explain why more women with GDM had this risk factor. Although a greater proportion of women with GDM diagnosed by the first OGTT had this risk factor compared with those diagnosed by the second OGTT, this did not reach statistical significance.

In this study, only 2-hour PG but not FPG or HbA1c at first OGTT could identify women with pre-GDM or early-onset GDM. Since early diagnosis of GDM allows early commencement of lifestyle modification and treatment before development of adverse pregnancy outcomes and diabetic complications, this finding confirmed that OGTT in early pregnancy could not be omitted based on FPG and HbA1c.

In women without GDM in early pregnancy, first HbA1c was not useful in predicting or excluding GDM in the later stage of pregnancy. This could be explained by the fact that HbA1c in early pregnancy reflects the degree of glycaemia in the preceding few months, which is expected to be normal if the early pregnancy OGTT is normal. The HbA1c results may also be affected by haemoglobinopathies, which are prevalent in our local population. Cost and standardisation of HbA1c testing are also issues for consideration[9].

Fasting plasma glucose is commonly used as a screening test for GDM. There is no consensus on its optimal cutoff value, which varies among different studies[14-16]. In Hong Kong, the optimal value for low-risk populations was suggested to be 4.1 mmol/L[17], which is lower than that in international studies. In a study on high-risk populations in Hungary, the cutoff value of FPG alone in early pregnancy was 5.0 mmol/L, above which a significantly increased risk of subsequent GDM was noted[13]. The cutoff value for FPG in this study was lower and compatible with that in a previous local study[18], but a significant number of GDM patients would be missed if it was used to screen high-risk women. Moreover, both the sensitivity and NPV of the cutoff values in the Hungarian study[13] were more than 90%, which were higher than any cutoff in our study. It is known that FPG has limited use in the Asian population because it identifies only a small proportion of women with GDM even when it is obtained at the time of OGTT[19]. Therefore, it is unlikely that early FPG is useful in predicting GDM, which is consistent with the findings in this study.

A study in non-pregnant population showed that when 2-hour PG fell below FPG, the risk of developing type 2 DM after 8 years of follow-up was lower, when compared with that in patients whose 2-hour PG remained higher than FPG[20]. Although all the women with 2-hour PG lower than FPG at the first OGTT in this study were in non-GDM group at second OGTT, the number was too small to make any reliable conclusion. Further studies investigating the change in glucose level after glucose load in pregnancy may be useful in identifying women who are at risk of progression to GDM in the current pregnancy.

The cutoff value for 2-hour PG was lower in this study compared with that in the Hungarian study (4.4 mmol/L vs. 6.2 mmol/L)[13]. Although it achieved the same sensitivity and NPV, fewer OGTTs were spared, which limited its use in the clinical setting. Given the high incidence of GDM in the high-risk group, small number of OGTTs spared in comparison with all women requiring OGTT, and the minimal risk associated with performing OGTT, the practice of repeating OGTT in the high-risk group should not be abandoned. However, in individual women who decline a repeated OGTT, we may consider omitting the second OGTT if results of the first OGTT do not exceed the cutoff criteria.

New World Health Organization Criteria

The high FPG cutoff value used in the 1999 WHO criteria[21] has been challenged as a majority of women with elevated FPG also had elevated 2-hour PG. Moreover, the criteria were extrapolated from non-pregnant populations and, hence, may not correlate with adverse pregnancy outcomes. The IADPSG proposed new criteria based on continuous graded relationships between higher maternal blood glucose levels and increased frequency of adverse

Table 8. 2013 World Health Organization criteria for diagnosing GDM and DM in pregnancy[22]*

	GDM	DM in pregnancy
75 g OGTT	-	-
FPG	5.1-6.9 mmol/L	≥7.0 mmol/L
1-Hour PG†	≥10.0 mmol/L	-
2-Hour PG	8.5-11.0 mmol/L	≥11.1 mmol/L
Random glucose	-	≥11.1 mmol/L (in the presence of diabetes symptoms)

Abbreviations: DM = diabetes mellitus; FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; OGTT = oral glucose tolerance test; PG = post-glucose

* Diagnosis made if ≥1 glucose value met

† There were no established criteria for the diagnosis of DM based on the 1-hour PG

pregnancy outcomes, based on data predominantly from the HAPO (Hyperglycaemia and Adverse Pregnancy Outcome) study[9]. Because of the emergence of new evidence, the WHO recently published new diagnostic criteria for hyperglycaemia first detected in pregnancy, distinguishing between diabetes and lesser degrees of glucose intolerance in pregnancy (Table 8)[22]. Although the definition of GDM applies at any time during pregnancy, it is uncertain whether early OGTT is beneficial and cost-effective. Moreover, FPG cutoff value of 5.1 mmol/L might lead to overdiagnosis of GDM in non-obese women. Nevertheless, both the WHO and IADPSG recommend a FPG value of ≥5.1 mmol/L at first antenatal visit to diagnose GDM, and performing 75 g OGTT at 24 to 28 weeks if FPG was <5.1 mmol/L[9,22].

It is estimated that the number of cases with DM in pregnancy or GDM will be increased by 50% if the new diagnostic criteria are applied[22]. Since 1-hour PG sample was lacking in this study, direct comparison of the two criteria was not possible. In this study, the number of GDM cases detected by the 2013 WHO criteria[22] was lower than that by the 1999 WHO criteria if only the FPG and 2-hour PG were used. It is likely that 1-hour PG will pick up the remaining cases of GDM. Lowering the FPG cutoff value will increase its sensitivity in detecting GDM, but raising the 2-hour PG cutoff will decrease its sensitivity. Among those with GDM diagnosed by first OGTT in this study, the mean FPG in early pregnancy was <5.1 mmol/L but the mean 2-hour PG was >8.5 mmol/L. Fasting plasma glucose alone was not useful in detecting early-onset GDM. Moreover, it is unlikely that all cases of GDM will be detected by the first OGTT. Therefore, among high-risk women, early OGTT is useful to detect early-onset GDM, and it is likely that second OGTT will be required, even if the 2013 WHO criteria[22] are adopted.

Limitations

Oral glucose tolerance test has been challenged for its reproducibility, as the intra-individual variation may be up to 10% to 30%. The application of the cutoff value in this study is limited to units using the same laboratory assays and similar protocol for screening GDM. Future prospective studies with bigger sample size should be performed to validate the findings. Future studies should also aim at defining cutoff values that address pregnancy outcomes, in particular macrosomia, as it is more important than a laboratory diagnosis of GDM. It is estimated that the prevalence of GDM will be 50% higher if the new WHO criteria are adopted. Future studies with 1-hour PG data are required and the impact of the new criteria on pregnancy outcomes in the local population is yet to be determined.

Conclusion

In the group of patients with two or more risk factors, formal OGTT in early pregnancy cannot be omitted because FPG and/or HbA1c are not useful to screen for GDM. This is valid even if the 2013 WHO criteria[22] are adopted in the local population. An OGTT should replace the use of FPG or HbA1c to screen for GDM at first antenatal visit as suggested by the IADPSG. Although second OGTT might be omitted in up to 5.3% of patients with two or more risk factors, the number was small in comparison with all women requiring OGTT. Therefore, the practice of performing a repeated OGTT in this group should continue. However, in individual women who decline a repeated OGTT, we may consider omitting the second OGTT if the first 2-hour PG is <4.4 mmol/L in the absence of onset of new risk factor(s) after the first OGTT.

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